Journal of Orthopaedics, Trauma and Rehabilitation 19 (2015) 83–88

Contents lists available at ScienceDirect

Journal of Orthopaedics, Trauma and Rehabilitation

Journal homepages: www.e-jotr.com & www.ejotr.org

Original Article

Surgical Difficulties and Complications in the Treatment of Bisphosphonate-related Proximal Femur Fractures
非典型股骨近端骨折外科手術的困難和併發症

Ma Chun-Man*, Cheung Man-Hong, Wong Wah-Bong

Department of Orthopaedics and Traumatology, North District Hospital, Sheung Shui, New Territories, Hong Kong

ARTICLE INFO

Article history:
Received 2 April 2014
Received in revised form
28 May 2014
Accepted 17 June 2014

Keywords:
bisphosphonate
fracture
intraoperative complications
postoperative complications

ABSTRACT

Background: Atypical proximal femoral fractures are becoming more common. They are difficult to treat because of the poor union rate and potential surgical difficulties due to hard bone and complete obliteration of the medullary canal.
Methods: This is a case series of five patients with bisphosphonate-related atypical proximal femur fractures. The study period was between June 2012 and October 2013. The patients were treated using cephalomedullary devices. The intraoperative difficulties and postoperative complications were recorded.
Results: We noticed complete femoral canal obliteration in two cases that required a set of addition reamers to reach the medullary canal. Moreover, the nonunion was 100% in the patient treated with standard nail and 25% in patients treated with long nail, and these nonunion rates were much higher than ordinary fractures.
Conclusion: Treatment of atypical femoral fractures can be difficult. Thus, proper preparations and expertise are required. Additional medical therapies may also be beneficial.

中 文 摘 要

非典型股骨近端骨折正變得越來越普遍。因其低的癒合率，治療並不容易。由因受影響的骨幹會硬化甚或出現骨髓腔完全閉塞，為手術帶來潛在的困難。本個案系列記載從2012年6月至2013年10月連續五位由雙膦酸鹽引至非典型股骨近端骨折在本院醫治的病人。他們都接受了頭骨髓腔(cephalomedullary)髓內釘固定手術。術中的困難和術後併發症都被紀錄。在兩個個案中，因股骨髓腔完整閉塞，我們需要用一組額外的鉸刀才能把守打通。此外，在標準髓內釘的個案中，骨折不癒合率為100%。使用長髓內釘的個案也有25%的不癒合率。比起普通的股幹骨折，這明顯要較高。總括而言，非典型股骨骨折的治療是困難的。對此要有適當明瞭及術前準備。使用其他藥物也可能是有益的。

Introduction

Proximal femur fractures related to prolonged bisphosphonate use are not uncommon. However, the treatment outcomes, especially the union rate, are much inferior to those of ordinary femoral fractures.[1,2] Moreover, they are more technically challenging because of hard bone and obliteration of the medullary canal.[3] However, there are only a few reports about the difficulties encountered during surgery and the treatment options for these fractures. In this case series, we will review the intraoperative difficulties and postoperative complications in treating atypical proximal femoral fractures using cephalomedullary devices.

Methods

From June 2012 to October 2013, five patients were admitted to North District Hospital, Sheung Shui, Hong Kong with atypical femur fracture. The diagnoses of atypical fractures were based on the American Society for Bone and Mineral Research criteria (Table 1).[4] All patients received bisphosphonate (alendronate) therapy and the duration of therapy varied from 3 years to 15 years. The fractures were located in the subtrochanteric region within 5 cm below the

* Corresponding author. *E-mail:* cm_ma@hotmail.com.

http://dx.doi.org/10.1016/j.jotr.2014.06.002

lesser trochanter. One patient suffered from bilateral simultaneous fractures. The patients were treated operatively using cephalomedullary devices with a traction table and intraoperative fluoroscopy. The demographic features, durations of bisphosphonate therapy, any prodromal symptoms, intraoperative difficulties, nailing devices used, and the surgical complications were recorded.

Results

The mean age of the patients was 63 years and all of them were women. All patients received bisphosphonate (alendronate) and the mean duration of therapy was 7.4 years (range, 3–15 years). The mean duration of follow-up was 16 months (range, 6–22 months). The follow-up period for individual patients is shown in Table 2. Thigh pain was the presenting symptom in three of the five patients and the other two patients suffered from fractures after a fall injury on level ground. All the fractures were fixed with long cephalomedullary nails except in one patient with bilateral simultaneous fractures, in whom standard nails were used.

Difficulties encountered during the surgeries included hard bone in all cases and complete obliteration of the proximal medullary cavity in two cases. Power drillings were required to open the femoral canal and serial hand reamers (starting from 6 mm) were used to serially dilate the tract before using the cannulated awl to reach the medullary canal in the shaft (Figure 1). The reaming rod was then inserted. For all patients, the calcium and phosphate levels were normal and the reaming materials were negative for malignancy.

For the only patient treated with 9-mm diameter standard nails (Figure 2), nonunions were observed in all the fractures. At 9 months after the operation, the nails on the left were broken just proximal to the distal locking screw (Figure 3) and revision fixation with long nail was performed. For the right side, dynamization by removal of the distal locking screw together with bone morphogenetic protein application was performed. Consolidation of the fracture was seen at the side on which revision fixation was performed using the long nail but not on the other side at 9 months after the second operation (Figure 4). The patient complained about mild pain over the right thigh but this did not affect her walking status or daily functions. The pain improved at the end of the study period. The wound healed well and serial X-rays up to the last follow-up showed similar alignment with no further lateral migration at the distal end or implant failure. The white cell count, erythrocyte sedimentation rate, and C-reactive protein level remained within normal limits. However, the persistence of nonunion with prominent fracture gap was noted over the right side and solid union was noted on the revision side (Figures 5 and 6). Revision fixation using the long nail was suggested but it was declined as she was concerned surgical complications. Injection of teriparatide was also offered to promote bone healing but she refused again after her discussion with endocrinologist due to the remote risk of osteosarcoma.

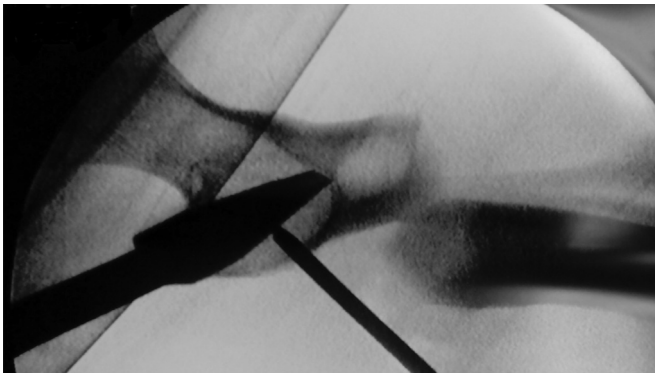

Figure 1. Intraoperative X-ray showing complete obliteration of proximal intra-medullary cavity.

Table 1
American Society for Bone and Mineral Research criteria for diagnosing atypical femoral fractures.[4]

Major features*	Minor features
No history of trauma, or fractures associated with low-energy trauma†	Localized periosteal thickening of the lateral cortex
Fracture located anywhere from distal to the lesser trochanter to proximal to the supracondylar area	Generalized thickening of the femoral cortices
Transverse or short oblique fracture configuration	Prodromal symptoms
Noncomminuted fracture	May be associated with bilateral fractures or symptoms
Medial spike in complete fractures; incomplete fractures involve only the lateral cortex	Evidence of delayed fracture healing
	Comorbid conditions or the use of some medications‡

* All major features, accompanied by none or some of the minor features, are required to diagnose atypical femoral fractures.
† Low-energy trauma is defined as a fall from a standing height or less.
‡ Examples of comorbid conditions and medications are rheumatoid arthritis, rickets and osteomalacia, renal osteodystrophy, and the use of bisphosphonates, glucocorticoids, or proton-pump inhibitors.

Table 2
Summary of clinical features of patients, treatments, and complications.

Patient no.	Age (y)	Sex	Duration of alendronate (y)	Presentation	Side(s) of the fracture:bilateral/unilateral	Sizes and brands of cephalomedullary devices	Duration of follow-up (mo)	Additional medical therapy	Complications
1	63	F	3	Minor fall	Bilateral	9 mm × 240 mm for both sides. PFNA from Depuy Synthes	22	Nil	Nonunion at 9 mo with broken nail on one side
2	82	F	6	Thigh pain	Unilateral	10 mm × 340 mm. Long gamma nail from Stryker	19	Nil	Nonunion with fracture distal locking screw at 1 y
3	79	F	5	Minor fall	Unilateral	10 mm × 360 mm. Long gamma nail from Stryker	19	Strontium ranelate	Nil
4	73	F	8	Thigh pain	Unilateral, incomplete on the right side	10 mm × 340 mm. Long PFNA from Depuy Synthes	14	Strontium ranelate	Nil
5	66	F	15	Thigh pain	Unilateral	10 mm × 300 mm. Long PFNA from Depuy Synthes	6	Nil	Nil

PFNA = proximal femoral nail antirotation.

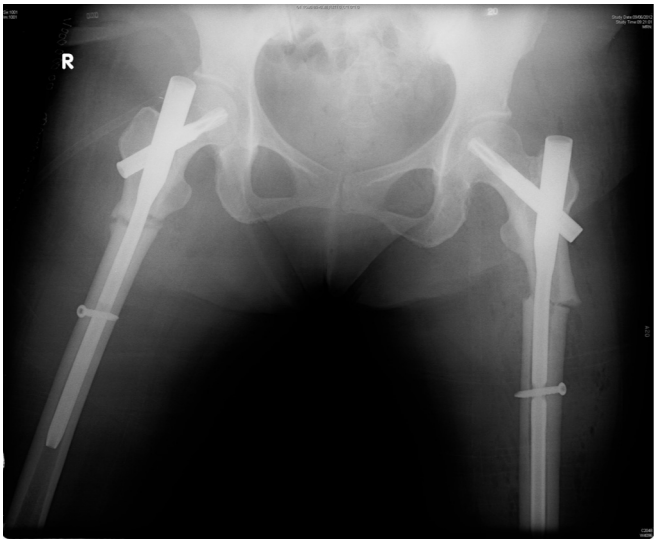

Figure 2. Anteroposterior X-ray showing fixation of atypical fractures using standard nails.

For the patients treated with long nails, fractures in 75% of the patients healed in 6 months. One case of nonunion with fracture distal locking screw was seen at 1 year after the operation (Figure 7). This patient was treated with revision fixation using a thicker long nail and the fracture healed 3 months after the revision surgery (Figure 8).

Discussion

Bisphosphonate is a commonly used drug for osteoporosis. It helps to increase the bone mineral density by inhibiting osteoclast activities, and therefore, it can severely suppress the bone turnover

Figure 3. Postoperative X-ray showing breakage of the nail proximal to the distal locking screw.

Figure 4. Anteroposterior X-ray at 9 months post-operation. Consolidation of fracture was seen on the left but non-union was found on the right.

in long-term users.[5] It can also lead to microdamage accumulation, which impairs stress-fracture healing, a reduction in matrix heterogeneity, and an increase in advanced glycation end products.[6] Although the bone quantity is improved, the bone quality is worsened.

The bisphosphonate-related subtrochanteric fracture is difficult to treat surgically and heal biologically. The subtrochanteric region is defined as the area within 5 cm below the lesser trochanter and it consists mainly of cortical bone. The healing involves primary cortical healing and is slow to consolidate. The healing is further compromised in the case of atypical fractures.[7]

Figure 5. Anteroposterior X-ray showing fracture healing on the left side but non-union on the right.

Figure 6. X-ray showing healing of the fracture on the left side.

The fracture is displaced during the flexion, abduction, and external rotation of the proximal fragment because of the strong muscle pull by the iliopsoas and abductors. The distal fragment is displaced in the adducted direction due to the action of the adductor muscles. Understanding these deforming forces is essential because accurate reduction of fracture gap is the most important factor to offload the high stresses in these load-sharing implants to prevent hardware failure and subsequent nonunion.[8]

The fracture gap can be significantly reduced by aligning the distal fragment with the abduction and flexion, which is achieved by elevating and externally rotating the boot on the traction table.

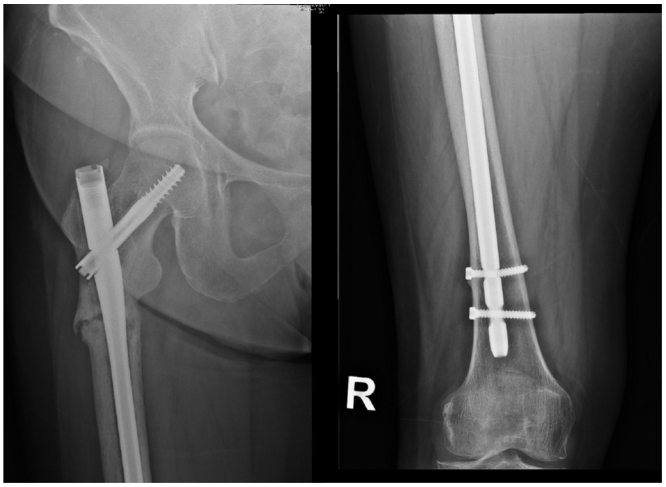

Figure 7. X-rays taken at 1 year post-operation showing non-union with breakage of the distal locking screw.

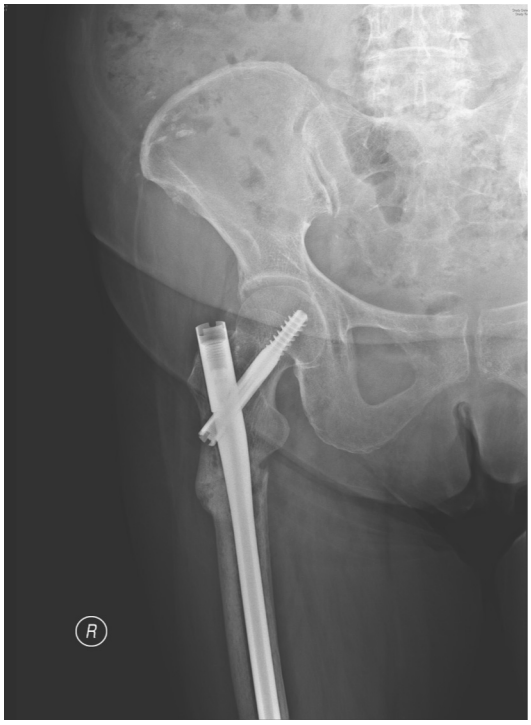

Figure 8. Fracture healing 3 months after the revision surgery.

Buttock support can also reduce the degree of external rotation of the proximal fragment. An F wrench may be used to control the anteroposterior or medial–lateral malalignment. Lateral position rather than making the patient lie on traction table provides a greater degree of freedom for the distal fragment to align with the proximal fragment. However, the intraoperative fluoroscopy screening is more difficult and additional assistance is required in maintaining the alignment.

If the fracture cannot be satisfactorily reduced, mini-open methods can be used. The joystick technique involves inserting a Schanz screw over the calcar region to control the deformation of the proximal fragment. Care must be taken to avoid injury to the femoral neurovascular bundle while performing blunt dissection into the bone before screw insertion. A ball spike pusher over the lateral aspect of the tip of the abducted fragment can also be used in difficult cases. These methods can be used either alone or in combination. A fracture reducer, like a short intramedullary nail with small canal diameter, can be inserted into the canal of the proximal fragment and this can act as a joystick to flex, adduct, and internally rotate the proximal fragment.[9]

The universal distractor can also be used to apply reduction forces that will improve fracture reduction through the effects of the soft-tissue envelope. The need for bone grafting can be reduced by applying these indirect reduction techniques.[10]

Open reduction, in case of persistent malalignment, should be performed as gently as possible to avoid significant periosteal stripping.

Although most published studies reported about the post-operative complications, only a few have reported about the intraoperative difficulties.

The case report by Lim et al[3] mentioned about the femoral canal obliteration secondary to prolonged alendronate use. They encountered difficulties while inserting the long guide wire due to hard bone. As a result, the fracture site was explored and the medullary canal was recreated by drilling. In our series, we

encountered two cases with the same problem. We can successfully create the canal for the reaming rod by the closed method using serial hand reamers in the flexible reamer set for intramedullary nails (DePuy Synthes). They are small enough to create the canal serially and long enough to reach even the mid femoral shaft. The open method can be avoided to preserve periosteal blood supply. These long and thin reamers should be prepared because they are not provided in the commonly used set (Gamma nail from Stryker (Kiel, Germany) and Proximal femoral nail antirotation from Depuy Synthes (Oberdorf, Switzerland)). The reaming device required insertion of guide wire or guide pin, which may not be possible in case of hard bone and obliteration of canal. Obliteration of femoral canal can be difficult to appreciate before the operation. Although the medullary bone inside the canal is hardened, it is still less dense than the cortical bone. Therefore, the cortex and medullary cavity can still be differentiated in the preoperative X-rays. Figures 9 and 10 show the injury films of the patient with obliteration of canal found intraoperatively (Figure 1). By the time some of the hard trabecular bone is removed from the proximal femur intraoperatively, the distinction can be revealed under fluoroscopy (Figure 1). The aforementioned hand reamer is used if complete obliteration occurs. In that situation, the reaming rod cannot be passed into the distal part of the femur even after opening the cortex at the tip of greater trochanter. The cannulation procedure is first performed using hand reamer and pneumatic reaming can be started after successfully placing the reaming rod.

The reported overall complications can be up to 68% according to a review by Prasarn et al.[1] There was a 25% nonunion in the study by Das De et al.[11] Weil et al[2] showed that secondary procedures were required in 44% of the patients treated with intramedullary nail fixation due to impaired bone healing. In a series of 17 fractures treated with long cephalomedullary nails, fracture healing was seen in only 54% of the patients and 46% of them required revision surgery.[2] In a recent study by Teo et al,[12] 33% of the patients required revision surgery and implant failure was observed in 23% of the patients. Increased complications rate in our study compared with previous studies could be due to heterogeneity of treatments, and the high complication rate (100%) associated with using short nails affected the overall rate. The small sample size would also affect the significance of our study.

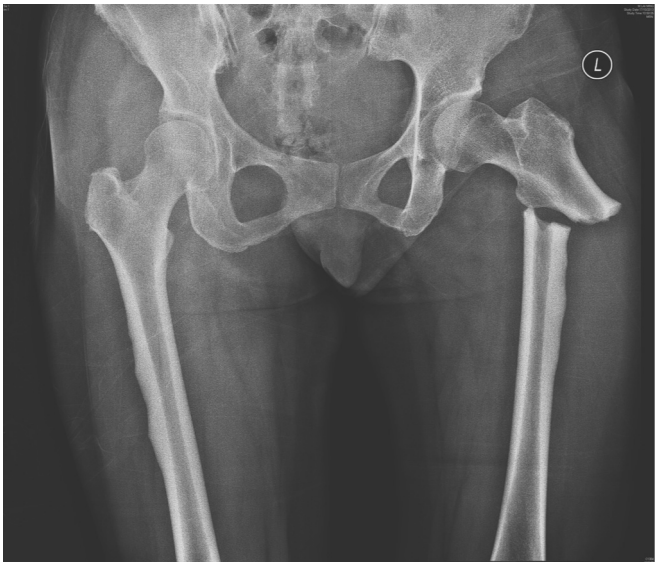

Figure 9. Anteroposterior X-ray showing atypical fracture on the left. Obliteration of canal cannot be seen.

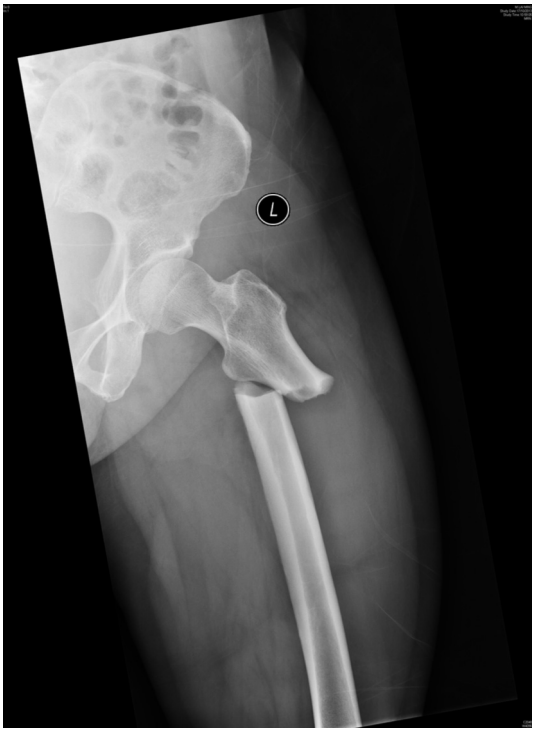

Figure 10. Lateral X-ray of the same patient in which obliteration of the canal is difficult to appreciate.

At present, there is still no prospective controlled trial about the guidelines for treatment of fractures related to long-term bisphosphonate use.[6] The well-established treatment principle of femoral factures recommends early and stable fixation to allow for early mobilization and prevent the complications related to bed rest. However, there should be more considerations in case of atypical fractures because of their relatively high delay in healing or high nonunion rate. Identifying measures to increase implant stability and methods to promote bone healing and observe for sequential fracture in the contralateral femur will be useful in this regard.

The choice of ideal fixation implant for atypical subtrochanteric and femoral shaft fractures is still under evaluation and there is no international guideline available on this yet.[4] For a patient with typical subtrochanteric fractures, short cephalomedullary devices were found to be a safe alternative to longer nails.[13] For atypical femoral fractures, there was a case report about the success of using the standard cephalomedullary device, but the time to union was 18 months.[14]

In patients with atypical femoral fractures, the fracture healing is impaired due to inhibition of osteoclastic remodelling and the entire femur is diseased. The use of long nail improves the working length of the fixation and can avoid increasing the stress around the tip of the nail that may cause thigh pain or even develop into a fracture. The task force of the American Society for Bone and Mineral Research suggests the use of intramedullary reconstruction full-length nails to protect the whole femur. Moreover, the medullary canal should be over-reamed (at least 2.5 mm larger than the nail diameter) to compensate for the narrow intramedullary diameter, facilitate insertion of the reconstruction nail, and prevent fracture of the remaining shaft.[4] In our series, standard cephalomedullary nails were used because the fixations were judged to be stable enough by the attending surgeons. In retrospect, the use of long nail together with the aim for perfect reduction may have avoided the nonunion complications.

Two distal locking screws were inserted for the long nail to maintain rotation stability and leg length in our case series. Early dynamization for delay union can be performed by removing the static locking screw. In a study by Wu,[15] the union rate following removal of static screw was 58% but 21% of the patients developed shortening of lower limb by 2 cm. Additional procedures such as cancellous bone grafting or exchange nail were required for those with persistent nonunion.

For stable types of fractures such as those with transverse pattern or A3 type according to the AO classification, insertion of single distal locking screws over the proximal part of the dynamic hole can allow immediate fracture compression.[16]

To promote bone healing, bisphosphonate therapy should be stopped and calcium and vitamin D supplements should be started. The recommended daily intake for calcium is 1000–1200 mg[17] and 400–800 IU for vitamin D_3.[17] The use of anabolic agents such as teriparatide should also be considered to enhance fracture healing.[18–20]

Conclusion

Treatment of bisphosphonate-related proximal femoral fractures can be challenging. Surgical difficulties and complications can be minimized not only by better operative preparations and stable fixations, but also by postoperative surveillance and medical therapies.

Conflicts of interest

All contributing authors declare no conflicts of interest.

References

1. Prasarn ML, Ahn J, Helfet DL, et al. Bisphosphonate-associated femur fractures have high complication rates with operative fixation. *Clin Orthop Relat Res* 2012;**470**:2295–301.
2. Weil YA, Rivkin G, Safran O, et al. The outcome of surgically treated femur fractures associated with long-term bisphosphonate use. *J Trauma* 2011;**71**:186–90.
3. Lim CT, Setiobudi T, Das De S. Femoral canal obliteration secondary to prolonged alendronate use: a case report. *J Orthop Surg (Hong Kong)* 2012;**20**:115–7.
4. Shane E, Burr D, Ebeling PR, et al. Atypical subtrochanteric and diaphyseal femoral fractures: report of a task force of the American Society for Bone and Mineral Research. *J Bone Miner Res* 2010;**25**:2267–94.
5. Odvina CV, Zerwekh JE, Rao DS, et al. Severely suppressed bone turnover: a potential complication of alendronate therapy. *J Clin Endocrinol Metab* 2005;**90**:1294–301.
6. Unnanuntana A, Saleh A, Mensah KA, et al. Atypical femoral fractures: what do we know about them?: AAOS exhibit selection. *J Bone Joint Surg Am* 2013;**95**:e8.1–8.13.
7. Perren SM. Evolution of the internal fixation of long bone fractures. The scientific basis of biological internal fixation: choosing a new balance between stability and biology. *J Bone Joint Surg Br* 2002;**84**:1093–110.
8. Riehl JT, Widmaier JC. Techniques of obtaining and maintaining reduction during nailing of femur fractures. *Orthopedics* 2009;**32**:581–8.
9. Kim KC, Lee JK, Hwang DS, et al. Stabilizing subtrochanteric femoral fractures with an interlocked intramedullary nail using the 'joystick' technique. *Orthopedics* 2007;**30**:705–8.
10. Kinast C, Bolhofner BR, Mast JW, et al. Subtrochanteric fractures of the femur. Results of treatment with the 95 degrees condylar blade-plate. *Clin Orthop Relat Res* 1989;**238**:122–30.
11. Das De S, Setiobudi T, Shen L, et al. A rational approach to management of alendronate-related subtrochanteric fractures. *J Bone Joint Surg Br* 2010;**92**:679–86.
12. Teo BJ, Koh JS, Goh SK, et al. Post-operative outcomes of atypical femoral subtrochanteric fracture in patients on bisphosphonate therapy. *Bone Joint J* 2014;**96-B**:658–64.
13. Chow CH, Chacko A, Rodriguez E, et al. Outcome of 3rd generation short cephalomedullary fixation of unstable intertrochanteric and subtrochanteric femur fractures in a geriatric population: preliminary results. *Orthop J Harv Med Sch* 2008;**10**:60–1.
14. Vaishya R, Vaish A, Nadeem A. Bisphosphonate-induced atypical subtrochanteric femoral fracture. *BMJ Case Rep* 2013 Nov 28;**2013**. http://dx.doi.org/10.1136/bcr-2013-201931. [Date of Electronic Publication: 2013 Nov 28].
15. Wu CC. The effect of dynamization on slowing the healing of femur shaft fractures after interlocking nailing. *J Trauma* 1997;**43**:263–7.
16. Raaymakers E, Schipper I, Simmermacher R, van der Werken C, Baumgaertner M. Reduction & fixation part for the proximal femur 31-A3 CRIF. https://www2.aofoundation.org/wps/portal/surgery/. [Last accessed date: March 2014].
17. Ross CA, Taylor CL, Yaktine AL, et al. *Dietary reference intakes for calcium and vitamin D*. Washington, DC: National Academies Press; 2011. p. 1132.
18. Andreassen TT, Ejersted C, Oxlund H. Intermittent parathyroid hormone (1-34) treatment increases callus formation and mechanical strength of healing rat fractures. *J Bone Miner Res* 1999;**14**:960–8.
19. Andreassen TT, Fledelius C, Ejersted C, et al. Increases in callus formation and mechanical strength of healing fractures in old rats treated with parathyroid hormone. *Acta Orthop Scand* 2001;**72**:304–7.
20. Holzer G, Majeska RJ, Lundy MW, et al. Parathyroid hormone enhances fracture healing. A preliminary report. *Clin Orthop Relat Res* 1999:258–63.